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Ronald L. Wilson, Director
Health Assessment Policy Staff
Office of Health Affairs (HFY-20)
Food and Drug Administration
5600 Fishers Lane, Room 15-22
Rockville, MD 20857

Re: GEMZAR®

FDA Docket No. 96E-0314

Dear Mr. Wilson:

Transmitted herewith is a copy of the application for patent term extension of U.S. Patent No. 4,808,614. The application was filed on July 12, 1996, under 35 U.S.C. § 156, but was dismissed in a decision dated March 14, 1997 because gemcitabine, a product claimed by the above-identified patent, was not considered to be an active ingredient of GEMZAR®. On reconsideration, the above-identified patent is considered to be eligible for patent term extension under 35 U.S.C. § 156 based upon the regulatory review period of GEMZAR®.

On August 14, 1997, applicant filed a response to the decision, arguing, among other things, that gemcitabine is an active ingredient of GEMZAR® as defined by 21 CFR 60.3(b)(2). As explained in the Product Information Sheet, page 2, column 2 (Exhibit 1 to the Application for Patent Term extension), 200 mg of the human drug product GEMZAR® is to be reconstituted with 25 mL of 0.9% Sodium Chloride Injection for intravenous administration to a patient. GEMZAR® contains gemcitabine hydrochloride, which, when diluted, dissociates into gemcitabine. It is gemcitabine which the product information sheet describes as the product which is metabolized by the body of the patient to yield other beneficial products. Accordingly, the product information sheet indicates that this dilution yields a gemcitabine concentration of 40mg/mL, which may be further diluted. The product information sheet continues to explain the storage conditions and stability of reconstituted GEMZAR®. The therapeutic effect of a reconstituted product may vary depending upon how the reconstituted product is stored. Accordingly, approval by the Food and Drug Administration of GEMZAR® and of labeling that states that the product GEMZAR® is only to be administered intravenously and in a solution that contains gemcitabine is considered to be evidence that gemcitabine was also subject to regulatory review with gemcitabine hydrochloride.

To be eligible for patent term extension, the patent must claim a product that was subject to regulatory review by the Food and Drug Administration before its commercial marketing or use. 35 U.S.C. § 156(a)(4), *inter alia*. The term "product" is defined in 35 U.S.C. § 156(f)(2) as a "drug product," which is further defined to mean the active ingredient of a new drug. The term "active ingredient" is defined in 21 CFR 60.3(b)(2) as "(2) any component that is intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body of man or of animals. The term includes those components that may undergo chemical change in the

manufacture of the drug product and be present in the drug product in a modified form intended to furnish the specified activity or effect."

Gemcitabine is understood to be present in the drug product GEMZAR® in a modified form (i.e., as gemcitabine hydrochloride) and, accordingly, gemcitabine is understood to be an active ingredient for purposes of 35 U.S.C. § 156(f)(2).

The above-identified patent is considered to claim a product, gemcitabine, that was subject to regulatory review under the Federal Food, Drug and Cosmetic Act. Subject to final review, the subject patent is considered to be eligible for patent term restoration. Thus, should you agree, a determination by your office of the applicable regulatory review period is necessary. Accordingly, notice and a copy of the application are provided pursuant to 35 U.S.C. § 156(d)(2)(A).

Telephone inquiries regarding this matter should be directed to the undersigned at (703)306-3159.

Karin Tyson
Senior Legal Advisor
Special Program Law Office
Office of the Deputy Assistant Commissioner
for Patent Policy and Projects

cc: Margaret Brumm
Eli Lilly and Company
Patent Division/MMB
Lilly Corporate Center
Indianapolis, IN 46285

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